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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,743	07/03/2001	Krassen Dimitrov	011616-004-999	3666
20583	7590	02/01/2008		
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			EXAMINER CHUNDURU, SURYAPRABHA	
			ART UNIT	PAPER NUMBER
			1637	
			MAIL DATE	DELIVERY MODE
			02/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/898,743

Applicant(s)

DIMITROV, KRASSEN

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 90-178 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 90-178 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/13/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' response to the office action filed on December 05, 2007 has been considered and acknowledged.
2. The Information Disclosure Statement filed on December 05, 2007 has been considered and acknowledged.

Status of the Application

3. Claims 90-178 are pending. Claims 1-89 are cancelled. All arguments have been fully considered and thoroughly reviewed, but are deemed persuasive-in-part for the reasons that follow. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. This action is made FINAL.

Response to arguments:

4. With regard to the objection to the specification, Applicants' amendment and arguments have been fully considered and the objection is withdrawn herein in view of the amendment.
5. With regard to the interview summary, examiner herewith acknowledges the Applicants' statements.
6. With regard to the rejection of claims 90- 178 under 35 USC 103(a) as being obvious over Barbera-Guillem et al. in view of Tanke et al., Applicants' arguments were fully considered and found unpersuasive. Applicants' argue that the combination of the references do not render the instant invention obvious. Applicants' further argue that Barbera-Guillem et al. teach a dendrimer with multiple layers of functionalized nanocrystals comprising primary and secondary dots and does not teach more than one genedigit/antigenedegit attached to a single molecule and does not teach a molecular probe with a plurality of genedigits, at least two of which are attached to

respective anti-genedigit. Applicants also assert that Barbera-Guillem et al. teach primary and secondary dots with different sequences to detect more than one target, at the most two different genes with 2 distinguishable signals, which is nowhere near the 30 distinguishable signals, nor suggest how such a diverse populations of 30 or more unique labels are achieved. Applicants further assert that Tanke et al. does not remedy the deficiencies of Barbera-Guillem et al. Applicants' arguments are found unpersuasive. First, as noted in the MPEP 2145 One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Second, the rejection discussed that the combination of the secondary reference makes the composition of Barbera-Guillem et al. obvious to generate 30 or more unique labels. Third, with regard to the arguments on molecular probe with plurality of genedigits, at least two of which are attached to anti-genedigits, Examiner notes that the limitation is taught by Barbera-Guillem et al. As pointed out, the Fig. 3 of Barbera-Guillem et al., does comprise a molecular probe attached to primary dots, which comprise plurality of genedigits (nucleic acid sequence strands) at least two of which are attached to secondary dots having anti-genedigits. Thus Barbera-Guillem et al. teach all the limitations required by the instant claims except for 30 or more unique labels, and as discussed in the rejection the combination of Tanke et al. render the instant invention obvious to achieve 30 or more unique labels.

Applicants' also argue that Tanke et al. teach multicolor insitu hybridization, which utilizes simultaneous use of combitorial labeling and ratio labeling and even if Tanke et al. teach multiplicity of 48 or 96 or more labels the teachings of Tanke et al. is not applicable to modify

the composition of Barbera-Guillem et al. and assert that there is no reason to modify the dendrimer of Barbera-Guillem et al. with different fluorophores in different ratios of Tanke et al. to achieve intended use of dendrimer as signal amplification of Barbera-Guillem et al. and further assert that multiple labels of Tanke et al. are incompatible with Barbera-Guillem et al. form of multiplexing. Applicants' arguments are found unpersuasive. First, Applicants agree that Barbera-Guillem et al. teach multiplexing and detection of plurality of targets (at least two targets) with two distinguishable labels. Thus if the statement is true, it is compatible to modify the multiplexing with more than two distinguishable labels with different fluorophores in different ratios to achieve detection of more than two targets. Examiner notes that multiplexing is the key for modification of the method which would enhance the detection of more than two target genes with distinguishable labels. Thus the ratio labeling is compatible with Barbera-Guillem et al.

With regard to the arguments based on intended use of the dendrimers of Barbera-Guillem et al. not satisfactory with ratio labeling, and the dendrimer structure of Barbera-Guillem et al. would not preserve the ratios of the different fluorophores taught by Tanke et al. and the shorter probes of Barbera-Guillem et al. are not applicable with longer probes of Tanke et al. Applicants' arguments were found unpersuasive because it is noted that the dendrimer structures formed by multiple primary and secondary dots of Barbera-Guillem et al. are flexible in their movement in solution thus the movement of the dots is based on the complementarity of the genedigit/ antigenedigits, irrespective of the length of the probes thus based on the base pairing of genedigit/antigenedigit, different dendrimer structures are formed and the ratio labelling is permissible because of the flexibility in the movement of the dots is compatible to

mix the fluorophores in different ratios. Further as disclosed in Barbera-Guillem et al. complementarity is not with respect to full length probe, thus length of the probe used is not relevant to the instant context. Thus as discussed in the rejection it is obvious to modify the composition of Barbera-Guillem et al. with the ratio labelling of Tanke et al. to achieve more than two, or 30 or more unique labels.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637


SURYAPRABHA CHUNDURU
PRIMARY EXAMINER 1/31/08